Doc Code: AP.PRE.REQ

PTO/SB/33 (07-05)
Approved for use through xx/xx/200x. OMB 0651-00xx
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 2400.0240001/VLC/L-Z

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

on _____

Signature _____

Typed or printed name _____

Application Number	Filed
10/518,669	July 21, 2005

First Named Inventor: Ulrike Wachendorff-Neumann

Art Unit	Examiner
1616	Qazi, Sabiha Naim

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [X] attorney or agent of record. Registration number 42,385.
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

Vincent L. Capuano
Signature

Vincent L. Capuano
Typed or printed name

(202) 371-2600
Telephone number

1-17-08
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

[X] *Total of One (1) forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 6796
Wachendorff-Neumann *et al.*	Art Unit: 1616
Appl. No.: 10/518,669	Examiner: Qazi, Sabiha Naim
Filed: July 21, 2005	Atty. Docket: 2400.0240001/VLC/L-Z
For: **Fungicidal Combinations of Active Substances**	

Arguments to Accompany the Pre-Appeal Brief Request for Review

Mail Stop AF

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants hereby submit the following Arguments, in five (5) or less total pages, as attachment to the Pre-Appeal Brief Request for Review (Form PTO/SB/33). A Notice of Appeal is concurrently filed.

Arguments

Applicants respectfully traverse the rejections set forth with respect to claims 6-9 in the Office Action of October 31, 2007. Applicants contend that the Examiner has erred in concluding that the data in the specification and in Dr. Peter Dahmen's declaration do not show a synergistic effect for the claimed combination.

A. The Invention

The present invention claims a specific combination comprising fungicidally active compounds trifloxystrobin, prothioconazole and tebuconazole, which possesses a synergistic effect. None of the cited references disclose or teach the presently claimed three-compound combination that possesses a synergistic effect.

B. Synergistic Effect

1. Data in the Specification

(a) First Error

According to the Examiner, the data in the specification on page 11 does not show a synergistic effect because "[t]he difference in synergistic efficacy 78 and compound of formula 1 [trifloxystrobin] (efficacy 67) does not represent synergism." Office Action, p. 4. Applicants respectfully traverse.

First, the Examiner's methodology/calculation applied in determining synergism or a lack thereof is inconsistent with the definition of synergism provided by the Examiner. According to the Examiner, synergism means "the combined action of two or more agents . . . that is greater than the sum of the action of one of the agents used alone." Office Action, p. 9, citing *In re Luvisi et al.*, 144 USPQ 646. However, the Examiner compared the efficacy of the combination (78%) with the efficacy of trifloxystrobin (67%), one of the three components of the combination. The Examiner ***should have*** compared the efficacy of the combination (78%) with the ***sum*** of the efficacy (48%) of three fungicides at the same application rate as required by the Examiner's own definition of synergism. Thus, the Examiner has erred in analyzing the data in the specification.

As discussed in detail below, because the efficacy of the claimed combination (78%) is greater than the sum of the efficacy (48%) of three fungicides at the same application rate, the claimed combination demonstrates a synergistic effect.

The data on page 11 in the specification shows that when the *Pyrenophora teres* infested barley plants are treated with trifloxystrobin, prothioconazole or tebuconazole ***individually*** at an application rate of 100 g/ha, trifloxystrobin, prothioconazole and tebuconazole have an efficacy of 67%, 56% and 22%, respectively. When the infested barley plants are treated with ***a combination*** of trifloxystrobin, prothioconazole and tebuconazole at an application rate of 100 g/ha (containing trifloxystrobin 35 g/ha, prothioconazole 30 g/ha and tebuconazole 35 g/ha), the combination has an efficacy of ***78%***.

Assuming a linear dose-response correlation, when acting alone at an application rate of 35 g/ha, trifloxystrobin has an expected efficacy of 23% [(35/100) x 67%]; when acting alone at an application rate of 30 g/ha, prothioconazole has an expected efficacy of 17% [(30/100) x 56%]; and when acting alone at an application rate of 35 g/ha, tebuconazole has an expected

efficacy of 8% [(35/100) x 22%]. The sum of the ***expected efficacy*** of the three components acting alone at the application rate of 35 g/ha of trifloxystrobin, 30 g/ha of prothioconazole and 35 g/ha of tebuconazole is ***48%*** (23% + 17% + 8% = 48%).

Alternatively, and in addition to the mathematical calculation of synergistic effect presented above, the synergistic effect of the present invention can be explained as follows:

The data on page 11 in the specification shows that when acting alone at an application rate of 100 g/ha, each individual component of the combination, trifloxystrobin, prothioconazole and tebuconazole has an efficacy of 67%, 56% and 22%, respectively. Therefore, trifloxystrobin, with an efficacy of 67% at 100 g/ha, is the most effective fungicide in the combination.

While keeping the same application rate of 100 g/ha, but substituting 65 g of the most potent trifloxystrobin (67%) with 30 g of less potent prothioconazole (56%) and 35 g of much less potent tebuconazole (22%), the resulting three-component combination has an efficacy of 78%, much greater than that of even the most effective fungicide trifloxystrobin (67%) used alone at 100 g/ha. The improved efficacy can only be the result of a synergistic effect between the three components because in the absence of a synergistic effect, the resulting three-component combination would be expected to be less effective than that of trifloxystrobin (67%) used alone. Therefore, the three-component combination of trifloxystrobin, prothioconazole and tebuconazole as claimed in claims 6-9 has a synergistic fungicidal effect.

(b) Second Error

According to the Examiner, the data in the specification on page 11 does not show a synergistic effect because "[t]he data presented in the specification is not a isde [sic] by side comparison. The amounts g/ha is 100 for the compounds (I), (II) and (III) when there [sic] individual efficacies has been observed. However, when synergism according to present invention was calculated the amounts were 35+30+35. The ratios as disclosed are 10:8.5:10." Office Action, p. 6. Applicants respectfully traverse.

Assuming a linear dose-response correlation, the efficacy of trifloxystrobin at 35 g/ha is 35/100 of the efficacy at 100 g/ha, or 35/100 x 67% = 23%. Likewise, the efficacy of prothioconazole at 30 g/ha is 30/100 of the efficacy at 100 g/ha, or 30/100 x 56% = 17%, and the efficacy of tebuconazole at 35 g/ha is 35/100 of the efficacy at 100 g/ha, or 35/100 x 22% = 8%. In this way, a side by side comparison can be made between a combination of 35:30:35 (10:8.5:10) and each of the components in the combination at the same concentration.

As described above, when *Pyrenophora teres* infested barley plants are treated with ***a combination***, containing trifloxystrobin 35 g/ha, prothioconazole 30 g/ha and tebuconazole 35 g/ha, the combination has an efficacy of ***78%***. When *Pyrenophora teres* infested barley plants are treated with 35 g/ha trifloxystrobin alone, it has an expected efficacy of 23%; with 30 g/ha prothioconazole alone, it has an expected efficacy of 17%; and with 35 g/ha tebuconazole alone, it has an expected efficacy of 8%. The sum of the efficacy of the three components acting alone is ***48%***. Thus, contrary to the Examiner's assertion, Applicants have been making "a side by side comparison," i.e., trifloxystrobin 35 g/ha + prothioconazole 30 g/ha + tebuconazole 35 g/ha (35+30+35) in the combination versus trifloxystrobin 35 g/ha, prothioconazole 30 g/ha and tebuconazole 35 g/ha used alone (35:30:35). Thus, Applicants respectfully submit that the Examiner has erred in concluding that Applicants' calculation of synergistic effect is not "a side by side comparison."

2. Data in Dahmen's Declaration

Even though the Examiner acknowledged that example 2 in Dr. Dahmen's declaration shows the synergistic effect of the claimed combination, the Examiner concluded that example 1 in Dr. Dahmen's declaration does not show synergistic effect because "[i]n example 1 the calculated efficacy 67 and found 75 is not synergistic for *Blumeria graminis*." Office Action, p. 6. Applicants respectfully traverse.

The study described in example 1 of Dr. Dahmen's declaration shows the fungicidal effect of a combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. In this study, the wheat plants are first treated with trifloxystrobin, prothioconazole, or tebuconazole, or with a combination of trifloxystrobin, prothioconazole and tebuconazole. Then, *Blumeria graminis* fungus is introduced to the treated wheat plants to test the preventative (protective) effect of the fungicides. As shown in Table 1, when acting alone at an application rate of 3.3 ppm (parts per million), trifloxystrobin, prothioconazole and tebuconazole have an efficacy of 63%, 0% and 11%, respectively. According to the Colby formula, the calculated efficacy of the combination is 67%. However, the observed efficacy of the combination is 75%, greater than the calculated efficacy. Therefore, the combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. has a synergistic effect against *Blumeria graminis* fungus on wheat.

The Examiner questioned the validity of the Colby formula, citing *Ex parte Quadranti*. Office Action, pgs. 6 and 7. As quoted by the Examiner, the court in *Ex parte Quadranti* stated that "[t]here is no single, appropriate test for determining whether synergism has been demonstrated for chemical combination, rather, factors show in each case must be analyzed to determine whether chosen method has clearly and convincingly demonstrated existence of synergism or unobvious result." Office Action, p. 7. For the present invention, Applicants have clearly demonstrated the synergism of the claimed combination by using multiple methods. Applicants' showing of synergism docs not depend on the validity of the Colby formula alone.

C. Conclusion

As discussed above, the data in the specification and in Dr. Dahmen's declaration clearly shows a synergistic effect of the claimed combination at different ratios (1:0.85:1 and 1:1:1) and against different phytopathogenic fungi (*Pyrenophora teres*, *Blumeria graminis* and *Fusarium culmorum*). Applicants respectfully submit that the Examiner's conclusion that the claimed combination lacks synergism is a clear error. Applicants respectfully request that the rejections be withdrawn.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Vincent L. Capuano
Attorney for Applicants
Registration No. 42,385

Date: 1-17-08

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

SKGF_760355.1